ICD

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,821	12/03/2001	Ilan Sela	65558/JPW	1401

7590 03/18/2004

Cooper & Dunham
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,821	SELA ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *8,10,12,31 and 32* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,11,13-25 and 27-30* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3122002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-7, 9, 11, 13, 15-19, and 21-30 in the paper filed December 22, 2003 is acknowledged. The traversal is on the ground(s) that Groups I-VIII have overlapping claims, and that the differences in the groups appear to be a particular type of cell (response, page 6, 1st full paragraph). This is not found persuasive because the cell types of the different groups are special technical features that are not shared with each other. Further, considerations, such as the operability of the silencing system within a cell type, are also different for the different cell types. Applicants also argue that Groups IX-X are drawn to method of using the silencing system (response, paragraph bridging pages 6-7). During the course of examination, it was determined that it would not be an undue burden to further examine claim 20. Group IX was therefore rejoined with Group I. However, the method of Group X is distinct from the method of Groups I and IX. The method of Group X involves the use of random nucleic acid sequences, whereas the method of Group I uses nucleic acid sequences that has identity to a pre-determined target gene. Applicants also argue that it would not be a serious burden to examine all groups together, and that a search of the prior art for Groups II-X would not be a serious burden once the prior art for Group I is identified (response, page 7, 2nd full paragraph). However, as discussed above, the consideration of other issues, such as the operability of the system in the invention of Groups II-VIII and X, would be a serious burden.

Groups I and IX have been rejoined. It was also determined during the course of examination that it would not be an undue burden to further examine claim 14. Claims 1-7, 9, 11, and 13-30 have been examined in this Office action. The restriction requirement of Groups II-VIII and X is still deemed proper and is therefore made FINAL. Applicants are reminded to remove non-elected subject matter from the elected claims.

Information Disclosure Statement

2. The citation of the reference authored by Cox et al., Exhibit 12, was lined through in the IDS submitted March 12, 2002 because a date is not present. See 37 CFR 1.98 (b)(5).

Claim Objections

3. Claims 2, 5, 6, 7, 21, 26, and 29 are objected to for the following reasons

In claim 2, one of terms in the recitation, "said the" in line 6 should be deleted.

In claim 5: the term, --is-- appears to be missing in line 2 after "sequence".

In claim 6: the claim is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form. The claim attempts to limit the terminators of the silencing system of claim 1 or 2. However, claim 16 recites, "or any other suitable terminator capable of terminating the transcription..." This recitation does not limit the terminator of the parent claims.

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim attempts to limit the T7 promoter of claim 1 or 2 by indicating that it corresponds to the promoter sequence of the bacteriophage T7 of functional analogues thereof. The specification defines pT7 as being from bacteriophage T7, and therefore this recitation does not limit claim 1 or 2. Parent claims 1 and 2 do not mention any functional analogues of pT7. If the silencing system of claim 17 does not comprise the pT7 promoter, then it does not comprise all of the limitations of the claims from which it depends.

In claim 21: the article --a-- appears to be missing in the first line, before "plant".

Claim 26 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

In claim 29: the term, --to-- appears to be missing in line 2, after "corresponds".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-7, 9, 11, and 13-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 2, 3, 5, 19, 20, 21, 22, and 24-29: the term "substantially" renders the claims indefinite. It is not clear what is meant by this recitation. The term is a relative term that has no definite meaning, and makes the metes and bounds of the claims unclear.

Further in claim 1: the recitation, "a functional part thereof" in the last line renders the claim indefinite. The entire RNA or RNA transcript encodes the product of the target sequence. The specification, as discussed below, indicates that the silencing is occurring at the RNA level, that RNA transcripts of the target sequence cannot be detected. If the RNA transcript is cleaved, then the transcript will not produce its encoded product. It is then not clear what meant by the disappearance of "the functional part" of the RNA transcript, as opposed to the RNA transcript itself. It is suggested that the recitation be deleted from the claim, as it does not further define the invention and only adds confusion.

In claims 1, 2, 20, 21, 27, and 28: the recitation, "corresponding to the T7 RNA polymerase gene" renders the claims indefinite. It is not exactly clear what is meant by "corresponding." It is suggested that the recitation, "a nucleotide sequence corresponding to" be deleted.

In claim 5: the recitation, "identical or homologous" renders the claim indefinite. It is not exactly clear what the difference between the two terms is, in the context of the targeting sequence and target sequence. The silencing system of the invention silences target sequences that share identical sequences with the targeting sequence. It is not clear if Applicants intend "homologous" sequences to refer to differences between the target sequence and targeting sequence due to genetic code degeneracy. It is suggested that "or homologous" be removed from the claims.

In claim 6: the recitation, "the silencing of which is desired" renders the claim indefinite. It is not clear how this recitation aids in defining the claimed invention. A gene that one desires to silence may not be desired by another. It is suggested that the recitation be deleted.

In claims 6, 23, and 30: the recitation, "target sequence corresponds to" renders the claims indefinite. It is not exactly clear what "corresponds" refers to. The metes and bounds of the claims are unclear. It is suggested that "corresponds to" be replaced by --is--.

Further in claims 6, 23, and 30: the recitation, "or to a fragment thereof, within the scope of degeneracy of the genetic code" renders the claim indefinite. It is not clear what the recitation is attempting to limit. It is not clear what genetic code degeneracy has to do with the fragment. It is also noted that, parts a) and b) encompass differences due to genetic code degeneracy, since theses parts encompass all genes encoding all proteins, peptide products, and non-coding sequences.

Further in claims 6, 23, and 30: part d) of the claims render them indefinite. Part d) limits the target sequence to correspond to a nucleic acid sequence that hybridizes to any of the sequences of a)-c). However, parts a)-c) encompass any gene encoding any protein or peptide product, any non-coding sequence, and any fragment thereof within the scope of genetic code degeneracy. It is not clear how nucleic acid sequences of part d) are different from parts a)-c), or what nucleic acid sequences are encompassed by part d) that are not encompassed by parts a)-c). The metes and bounds of the claims are unclear.

In claim 13: the term, "optionally" renders the claim indefinite. It is not clear whether or not the additional regulatory elements are present in the claimed invention. If they are not, then the claim does not further limit claim 5. It is suggested that the term be deleted.

In claim 15: the recitation, "the plant promoter is p35S" renders the claim indefinite. The specification indicates that "p35S" is the CaMV 35S promoter (page 16, 1st full paragraph). p35S is not a plant promoter. It is suggested that the term, "plant" be deleted from the claim.

In claim 16: the claim introduces a narrowing limitation, "said terminators is the NOS terminator or a functional equivalent or fragment thereof, the B-1,3-gluconase terminator", but then recites a broader limitation: "or any other suitable terminator...". A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In claim 17: the recitation, "corresponds" renders the claim indefinite. It is not exactly clear what the meaning of this recitation is. It is suggested that the recitation, "corresponds to" be deleted.

In claims 22 and 29: the recitation, "substantially corresponds" renders the claim indefinite. It is not clear what targeting sequences are encompassed by this recitation. The metes and bounds of the claim are unclear.

In claim 25: the recitation, "carrying and expressing said silent target sequence" renders the claim indefinite. It is not clear what is meant by "carrying". The recitation also does not clearly indicate whether or not the target sequence is silent.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-7, 9, 11, 13-25, and 27-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards an expression silencing system comprising a nucleotide sequence corresponding to the T7 RNA polymerase gene or to a functional equivalent or fragment thereof which carry an NLS sequence, and a T7 promoter sequence or functional fragment thereof and at least one targeting sequence downstream of said pT7, which system is capable of rendering, upon introduction into a plant cell, the expression at the RNA level of a target sequence substantially silenced by causing the disappearance of the RNA or RNA transcript carrying said sequence or functional part thereof; or wherein said target sequence corresponds to a) a gene encoding any protein or peptide product, b) a non-coding nucleic acid sequence, c) a nucleic acid which corresponds to a) or b) or a fragment thereof, within the scope of genetic code degeneracy, or d) a nucleic acid which hybridizes with the sequence according to

a), b), or c) or a fragment thereof; or wherein said pT7 corresponds to the bacteriophage T7 promoter or functional analogues thereof; or wherein terminator sequences of said silencing system is the NOS terminator or a functional equivalent or fragment thereof; or a process for the transformation of a plant with said silencing system; or a method of silencing the expression of a target sequence within the genome of a plant, comprising said silencing system.

The specification indicates that the gene for the bacteriophage T7 RNA polymerase was fused to the translation enhancer element from Tobacco Mosaic Virus and a nuclear localization signal from SV40. This construct was operably linked to the CaMV 35S promoter and NOS terminator, and named "35S-T7-pol." Two constructs comprising the GUS coding sequence were made, both comprising said translation enhancer element. In one construct, the GUS coding sequence was fused to the 35S promoter and the NOS terminator, and the other comprised the T7 promoter and both the NOS terminator and T7 terminator. Figures 1A and 1B show diagrams of the constructs, and Figure 1C shows a diagram of a control construct comprising the GUS coding sequence fused to the 35S promoter and NOS terminator (page 16). The constructs were introduced into different tobacco or tomato plants via Agrobacterium, and homozygous plants were selected at the R2 generation. Transgenic plants comprising the T7 RNA polymerase construct, and which are capable of expressing GUS, were crossed with the transgenic plants comprising the T7-GUS constructs. The hybrid plants were self-pollinated and progeny selected for several generations. A 35S-T7-pol/pT7-GUS plant was pollinated with a plant expressing 35S-GUS. Three of the eighteen progeny plants comprised all three constructs, none of which expressed GUS. GUS expression also was not detected in the 35S-T7-pol/pT7-GUS plants, except for in the pollen grain and callus of two plants. GUS was not expressed, however, in the

leaves of those two plants. Nuclear run-on assays and RNAse protections assays indicated that GUS was being transcribed, but GUS mRNA was not accumulating in the cytoplasm (pages 18-20). Transgenic plants carrying the 35S-GUS construct were also crossed with the pT7-GUS plants, and the hybrid progeny selfed for several generations. A scion from a plant expressing the 35S-GUS construct was grafted onto the 35S-GUS/pT7-GUS silenced plants. Shoots growing from 3 of 6 grafter scions silenced for GUS (pages 20-21).

The claimed expression silencing system comprises nucleotide sequences corresponding to the T7 RNA polymerase gene or to a functional equivalent or fragment thereof. A review of the full content of the specification indicates that nucleotide sequences encoding the T7 RNA polymerase are essential to the operation of the invention.

The specification discloses only nucleotide sequences encoding the T7 RNA polymerase. Nucleotide sequences encoding functional equivalents or fragments of T7 RNA polymerase are not described. The Federal Circuit provided the appropriate standard for written description in *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997). The court held that a structural description of a rat cDNA was not an adequate description of broader classes of cDNAs, because a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." The court also held in *Lilly* that a genus of cDNAs could be described by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Here, the specification does

not provide any evidence on the record of a relationship between the structure of T7 RNA polymerase-encoding nucleotide sequences and the structures of functional equivalents or fragments thereof. No information is provided indicating the portions of T7 RNA polymerase that are essential to its functional activity, or the changes the can be made to the sequence of T7 RNA polymerase that would leave its RNA polymerase activity intact.

The claimed expression silencing system also comprises nucleotide sequences a pT7 sequence or any functional fragment or functional equivalent or analogue thereof.

The specification, however, does not disclose any functional fragments or functional equivalents or analogues of pT7. The specification does not describe any relationship between the structure of pT7 and any fragments thereof that retain its promoter activity. No information is provided that indicates the sequences of pT7 that are essential to its activity, or how the sequences of pT7 can be changed without affecting its activity.

Claim 16 also recites that the silencing system comprises the NOS terminator or a functional equivalent or fragment thereof. The specification, however, does not describe any functional equivalents of the NOS terminator, or any fragments thereof that retains its activity. The specification is silent as to the sequences of the NOS terminator that are essential to its function, and does not describe sequences that can be changed without changing its activity. Given the breadth of the claims and the description in the specification of only nucleotide sequences encoding T7 RNA polymerase, pT7, and the NOS terminator, it is submitted that the specification fails to provide an adequate written description of the multitude of nucleotide sequences and transgenic plants encompassed by the claims.

6. Claims 1-7, 9, 11, 13-25, and 27-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an expression silencing system comprising a nucleotide sequence encoding the T7 RNA polymerase, and pT7, does not reasonably provide enablement for functional equivalents or fragments of nucleotide sequences encoding T7 RNA polymerase, pT7, and the NOS terminator; the expression silencing system wherein the target sequence is a non-coding sequence in the plant genome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards an expression silencing system comprising a nucleotide sequence corresponding to the T7 RNA polymerase gene or to a functional equivalent or fragment thereof which carry an NLS sequence, and a T7 promoter sequence or functional fragment thereof and at least one targeting sequence downstream of said pT7, which system is capable of rendering, upon introduction into a plant cell, the expression at the RNA level of a target sequence substantially silenced by causing the disappearance of the RNA or RNA transcript carrying said sequence or functional part thereof; or wherein said target sequence corresponds to a) a gene encoding any protein or peptide product, b) a non-coding nucleic acid sequence, c) a nucleic acid which corresponds to a) or b) or a fragment thereof, within the scope of genetic code degeneracy, or d) a nucleic acid which hybridizes with the sequence according to a), b), or c) or a fragment thereof; or wherein said pT7 corresponds to the bacteriophage T7 promoter or functional analogues thereof; or wherein terminator sequences of said silencing system is the NOS terminator or a functional equivalent or fragment thereof; or a process for the

transformation of a plant with said silencing system; or a method of silencing the expression of a target sequence within the genome of a plant, comprising said silencing system.

The specification teaches the use of the T7 RNA polymerase/pT7 expression system in plants to silence a target sequence therein, as discussed above.

However, the specification does not teach functional equivalents or fragments of nucleotide sequences encoding the T7 RNA polymerase, pT7, or NOS terminator. The specification makes no mention of any functional equivalents of any of these elements. The specification and prior art are silent as to the sequences of any of these elements that can be changed without affecting their respective functional activities. Even minor changes in promoter sequences, for example, can have a drastic negative effect on its activity. Kim et al. (Plant Mol. Biol., 1994, Vol. 24, pages 105-117), for example, teach that deletions of a few nucleotides have a negative effect on the functional activity of the NOS promoter (pages 111-112). In the absence of further guidance, undue experimentation would be required by one skilled in the art to determine how the T7 RNA polymerase, pT7 promoter, and NOS terminator can be changed without affecting their functional activities.

The specification also does not enable the claimed invention when the target sequence is a non-coding sequence. The specification admits that the silencing induced by the claimed invention occurs at the RNA level, that the expression system allows transcription of the targeting sequence but that mRNA of the targeting sequence does not accumulate (page 9, 3rd full paragraph; pages 16-17). Post-transcriptional gene silencing affects the expression of transgenes and endogenous genes with which they share a high degree of sequence identity (reviewed, for example, in Stam et al., Ann. Bot., 1997, Vol. 79, pages 3-12). As the silencing is due to

homology shared between transcribed sequences, it is not clear, and not taught in the instant specification, how a non-coding sequence can be targeted with the claimed silencing system. In the absence of further guidance, undue experimentation would be required by one skilled in the art to determine how to use the claimed silencing system, which acts at the RNA level, to silence the expression of a target gene using non-coding nucleotide sequences. See Genentech, Inc. v. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention. Given the breadth of the claims, unpredictability of the art, and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-7, 13-15, 17, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Lassner et al.

The claims are broadly drawn towards an expression silencing system comprising a nucleotide sequence corresponding to the T7 RNA polymerase gene or to a functional equivalent

or fragment thereof which carry an NLS sequence, and a T7 promoter sequence or functional fragment thereof and at least one targeting sequence downstream of said pT7.

Lassner et al. teach a DNA construct comprising the nucleotide sequence encoding the T7 RNA polymerase operably linked to the double CaMV 35S promoter, a nucleotide sequence encoding the SV40 nuclear locator signal, and a transcription terminator sequence, and a DNA construct comprising the T7 promoter operably linked to nucleotide sequences of interest and a terminator. The constructs taught by the reference comprise the limitations of the elements of the DNA construct products encompassed by the claims. The property of silencing a target sequence, when present in a cell, which shares sequence identity with the nucleotide sequence operably linked to the T7 promoter is inherent to the T7 RNA polymerase/T7 promoter system taught by the reference. Claim 19 is included in this rejection, as it recites that the DNA constructs are "substantially" as shown in instant Figures 1A and 1B. Given the indefiniteness of the recitation, "substantially" (see the rejection above), the DNA constructs of the reference are substantially the same as those shown in the instant figures.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-7, 9, 13-17, 19-25, and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lassner et al. in combination with Blokland et al. (Plant J., 1994, Vol. 6, pages 861-877), and Palauqui et al. (EMBO J., 1997, vol. 16, pages 4738-4745).

The claims are broadly drawn towards an expression silencing system comprising a nucleotide sequence corresponding to the T7 RNA polymerase gene or to a functional equivalent or fragment thereof which carry an NLS sequence, and a T7 promoter sequence or functional fragment thereof and at least one targeting sequence downstream of said pT7, which system is capable of rendering, upon introduction into a plant cell, the expression at the RNA level of a target sequence substantially silenced by causing the disappearance of the RNA or RNA transcript carrying said sequence or functional part thereof; or wherein said target sequence corresponds to a) a gene encoding any protein or peptide product, b) a non-coding nucleic acid sequence, c) a nucleic acid which corresponds to a) or b) or a fragment thereof, within the scope of genetic code degeneracy, or d) a nucleic acid which hybridizes with the sequence according to a), b), or c) or a fragment thereof; or wherein said pT7 corresponds to the bacteriophage T7 promoter or functional analogues thereof; or wherein terminator sequences of said silencing system is the NOS terminator or a functional equivalent or fragment thereof; or a process for the transformation of a plant with said silencing system; or a method of silencing the expression of a target sequence within the genome of a plant, comprising said silencing system.

Lassner et al. is discussed above.

Lassner et al. do not teach crossing a first plant comprising a DNA construct comprising nucleotide sequences encoding the T7 RNA polymerase operably linked to a NLS, with a second plant comprising a DNA construct comprising the T7 promoter operably linked to a targeting

sequence, or the progeny of the cross comprising both constructs and in which a target sequence is silenced; or grafting.

Blokland et al. teach co-suppression of pigmentation of chalcone synthase (chs) in Petunia plants comprising a construct comprising the CaMV 35S promoter operably linked to a nucleotide sequence encoding a fusion of the uidA (GUS) gene and the chsA cDNA. Steady-state chs mRNA levels, and pigmentation, were reduced in the transgenic plants, including in flowers. GUS expression was also silenced in plant parts that were also silenced for chs. The constructs used also comprised nos terminator operably linked to the uidA/chs coding sequence (pages 862-866).

Palauqui et al. teach that silencing is transmitted with 100% efficiency from silenced rootstock, derived from transgenic plants that were co-suppressed for nitrate reductase and the uidA transgene, to grafted scions that were from transgenic plants that nitrate reductase and uidA (pages 4739-4742).

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to use the T7 RNA polymerase/pT7 system of Lassner et al. to silence genes of interest in plant cells, for example the chs gene of Blokland et al. It was obvious that the constructs comprising the TY RNA polymerase coding sequence, and pT7-target sequence could have been introduced into the same plant cell, and a transgenic plant regenerated therefrom; or into separate plant cell, wherein two transgenic plants would have been regenerated therefrom, and subsequently crossing the two plants to bring the two constructs into the same plant. Whether both DNA constructs were introduced into the same plant initially, or into different ones which were subsequently crossed, amounts to an optimization of process

parameters. It further would have been obvious that crossing the plant containing both DNA constructs to a non-transgenic plant that expresses the target sequence, would result in progeny plants that comprise both DNA constructs, and that the target sequence would have become silenced. It further would have been obvious to graft a plant, in which the target sequence sequence, for example chs, expressed its product, onto a rootstock from the transgenic plant comprising the two DNA constructs and wherein the targeting sequence, for example, was from the chs coding sequence. It would have been obvious, given the teachings of Palauqui et al., that the chs coding sequence would have become silenced in the grafted scion. One would have been motivated to use the T7 RNA polymerase/pT7 system to express a targeting sequence to silence a target sequence, given the teachings of Lassner et al. that this system successfully allows the transcription of nucleotide sequences operably linked to pT7 when in plant cells.

9. Claim 26 is objected to and was not examined on the merits. Claims 1-7, 9, 11, 13-25, and 27-30 are rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ashwin Mehta whose telephone number is 571-272-0803. The examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications and 703-872-9307 for After

Final communications. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 16, 2004

Ashwin D. Mehta, Ph.D.
Primary Examiner
Art Unit 1638